OPIOID INDUSTRY MEAL PAYMENTS AND ASSOCIATED PHYSICIAN PRESCRIBING

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Abstract

An extensive literature demonstrates a relationship between promotional activity towards physicians from drug manufacturers and subsequent prescribing of marketed products. A similar association has been demonstrated in a recent study focusing on opioid payments and opioid prescribing using multivariate linear regression (Hadland et al.) This article replicates this recent study by using updated meal payments and claims data and extends the research by examining whether a physician's specialty, gender, and geographic region of practice help better explain the relationship between opioid meal payments and prescribing. An association was found between opioid meal payments and opioid prescribing, which confirms prior study findings. The analysis found that specialty was an important predictor of opioid claims and that pain management specialists and physicians in rehabilitation-based specialties are associated with higher opioid claims. The analysis did not find evidence to suggest this relationship is different based on physician gender or region of practice.

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1. Introduction

The opioid epidemic is undoubtedly one of the most pressing health crises of our time, causing an estimated 72,000 deaths in 2017. In recent years, combatting the opioid epidemic with urgency has become a focus of the United States public policy. On October 26, 2017, President Donald Trump declared the opioid epidemic is a Public Health Emergency under federal law. Under this classification, the Secretary of the Department of Health and Human Services (HHS) can enact various far-reaching actions to help fight the opioid epidemic, including modifying various provisions that could re-allocate funds, personnel, and grants towards this public health issue. Even in our divided political environment, the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and Communities Act was passed by the United States Senate on October 3rd, 2018 with an overwhelming majority vote of 98 to 1. This act includes provisions to address treatment and recovery, prevention, protecting communities, and fighting fentanyl. While recent public policy actions by the US make it clear that fighting the opioid crisis is one of the nation's top public health concerns, do these actions address the causes of the opioid crisis?

While there are many factors that contribute to the opioid crisis, one of these factors is arguably the influence of the pharmaceutical industry through non-research marketing to physicians to influence their prescribing behavior. The link between pharmaceutical marketing and physician prescribing in general has been examined in numerous studies, but, there are few studies that have focused on opioids specifically. Due to the recent availability of Open Payments and Medicare Part D claims data to the general public from the Centers for Medicare and Medicaid Services (CMS), there has been an increase in analyses that have examined the relationship between pharmaceutical marketing and prescribing activity by joining these databases together, which provides a much more complete picture of this relationship available to the public than ever before.

The purpose of this analysis is to determine whether there is an association between opioid meal payments from PSRs to physicians and subsequent physician opioid prescribing. After establishing the nature of this relationship, subsequent analyses examined if understanding of this association could be enhanced through considering physician demographic characteristics like physician gender, state of practice, and specialty.

The findings of the analysis confirm that there is an association between opioid claims and opioid meal payments after controlling for non-meal payments and prior year opioid claims. The analysis found that specialty was an important predictor of opioid claims and that pain management specialists and physicians in rehabilitation-based specialties are associated with higher opioid claims. The analysis did not find much evidence to suggest this relationship is different based on the physician gender or region of practice.

2. Literature Review and Theoretical Framework

2.1. The Opioid Epidemic

For more than twenty years, the United States has been in the midst of an opioid epidemic. Opioids are a class of narcotics prescribed to patients experiencing acute or chronic pain that can either be derived from opium poppy plants or manufactured chemically. According to the World Health Organization (WHO), opioids have a high risk of dependence by users and overuse of opioids can result in respiratory depression and death. The rates of opioid overdose are increasing exponentially over time and this phenomenon is considered an epidemic by organizations like the US Food and Drug Administration (FDA) and US Disease Control and Prevention (CDC). This crisis imposes an irrefutable medical and economic burden on American citizens.

According to the CDC, drug overdoses were the leading cause of injury death in the United States in 2016. In 2016, there were 63,632 drug overdose fatalities and 42,249 (66.4%) of these deaths directly involved the use of opioids.[1] According to the CDC, there has been a 200% increase in opioid overdose fatalities between 2000 and 2014. This rate is accelerating compared to a 137% increase in overall drug overdose deaths during the same time period.[2]

In addition to costing many American citizens their lives, the opioid epidemic also yields a high monetary burden on the American economy. In 2013, Florence et al. estimated the opioid epidemic costs $78.5 billion annually based on health care, criminal justice, and loss of productivity costs. American taxpayers were estimated to have covered about 25% of these costs each year, which include both "direct services through government agencies, but also through tax revenue that will be lost from reduced earnings."[3] These monetary costs are likely to increase yearly unless there is a decline in opioid deaths, which is unfortunately counter to the current trend of increasing annual opioid-related fatalities.

The origins of the opioid epidemic are multifaceted and complex to derive, but the widespread nature of opioid prescribing for medical and non-medical use has been commonly traced to an increase of prescribing opioids for pain not related to cancer in the late 1990's and early 2000's. This change in prescribing behavior is believed to have been caused by patient advocacy for the use of opioids for non-cancer chronic pain, the perception that extended-release opioids like Purdue Pharma's OxyContin® were less addictive than prior opioid formulations, an easing of legal regulations that would have provided an avenue to prosecute physicians that wrote opioid prescriptions in high volumes, and an increase in marketing of opioid products by opioid manufacturers.[4]

1. Mattson, Christine L., PhD, Mbabazi Kariisa, PhD, Puja Seth, PhD, Lawrence Scholl, PhD, and Matthew Gladden, PhD. "Morbidity and Mortality Weekly Report (MMWR)." Centers for Disease Control and Prevention. August 30, 2018. Accessed October 02, 2018. https://www.cdc.gov/mmwr/volumes/67/wr/mm6734a2.htm?s_cid=mm6734a2_w.
2. Rudd, Rose A., Noah Aleshire, Jon E. Zibbell, and R. Matthew Gladden. "Increases in drug and opioid overdose deaths—United States, 2000–2014." American Journal of Transplantation 16, no. 4 (2016): 1323-1327.
3. Florence, Curtis, Feijun Luo, Likang Xu, and Chao Zhou. "The economic burden of prescription opioid overdose, abuse and dependence in the United States, 2013." Medical care 54, no. 10 (2016): 901.
4. Laxmaiah Manchikanti, M. D., I. I. Standiford Helm, Jeffrey W. Janata MA, Vidyasagar Pampati PhD, Jay S. Grider MSc, and P. DO. "Opioid epidemic in the United States." Pain physician 15 (2012): 2150-1149.

2.2. Pharmaceutical Payments Towards Physicians

While many Americans are likely familiar with direct-to-consumer advertising for pharmaceutical products on television that emerged in the US in the late 1990's, many citizens may not be aware of the history and continued dominance of pharmaceutical marketing budgets on the hiring and deployment of pharmaceutical sales representatives (PSRs) around the country dedicated towards the direct selling of their products to physicians through both in-person visits and telemarketing.[5] Despite the overall positive reception of PSRs by physicians and most physicians' perception that pharmaceutical marketing has no bearing on prescribing decisions, countless studies (of methodologies ranging from observational to randomized controlled trials) have established an association between physician marketing by PSRs and physician attitudes and prescribing behavior.[6]

One such study, a randomized controlled trial (RCT) by Grande et al. examined medical student attitudes towards pharmaceutical marketing, including level of skepticism, by exposing the students to Lipitor marketing promotions. Medical students were unaware the promotion was part of the study and students were either part of the University of Pennsylvania School of Medicine (UPenn), which restricts pharmaceutical marketing, or the University of Miami School of Medicine (Miami), which has less restrictive pharmaceutical marketing policies. The study found that Miami medical students held more favorable views and were less skeptical of pharmaceutical marketing than UPenn medical students due to their respective hospital policies on PSR drug promotion.[7] A more recent continuation of the literature examining the link between PSR marketing and physician attitudes was performed by Larkin et al. in 2017, which examined prescribing behavior of 2,126 physicians in 19 Academic Medical Centers (AMC) that reduced

5. Mackey, Tim K., Raphael E. Cuomo, and Bryan A. Liang. "The rise of digital direct-to-consumer advertising?: Comparison of direct-to-consumer advertising expenditure trends from publicly available data sources and global policy implications." BMC health services research 15, no. 1 (2015): 236.
6. Fickweiler, Freek, Ward Fickweiler, and Ewout Urbach. "Interactions between physicians and the pharmaceutical industry generally and sales representatives specifically and their association with physicians' attitudes and prescribing habits: a systematic review." BMJ open 7, no. 9 (2017): e016408.
7. Grande, David, Dominick L. Frosch, Andrew W. Perkins, and Barbara E. Kahn. "Effect of exposure to small pharmaceutical promotional items on treatment preferences." Archives of internal medicine 169, no. 9 (2009): 887-893.

access to PSRs between 2006 and 2012. The researchers found that physicians affiliated with hospitals with PSR-restrictive policies are associated with a 1.67% decrease in market share for products promoted by PSRs.[8]

When considering a broad approach to PSR marketing and physician prescribing, Fickweiler et al. published a systematic review that explored "interactions between physicians and the pharmaceutical industry including sales representatives and their impact on physicians' attitude and prescribing habits." Studies published between 1992 and 2016 were included if they involved PSRs engaging directly with the doctor and were excluded if they were qualitative, not published in an academic journal, and/or if they had a small sample size. Through the review of this literature, researchers found that physicians' "acceptance of gifts from the company's PSRs have been found to affect physicians' prescribing behavior and are likely to contribute to irrational prescribing of the company's drug."[6]

2.3. Physician Payments Sunshine Act

Comparatively lax regulation of PSR marketing payments to physicians, continued scrutiny of the relationship between PSR marketing and physician prescribing, and a US political environment conducive to passing healthcare reform led to the passage of the Physician Payments Sunshine Act (Sunshine Act) by the 111th US Congress as a part of the Patient Protection and Affordable Care Act (ACA) of 2010. The Sunshine Act necessitated the reporting of payments, transfer of value, or consulting fees (payments) that are greater than 10 US dollars by Group Payer Organizations (GPO), Physician-Owned Distributors (POD), and most drug and medical device manufacturers. These payments were first reported on March 31st, 2014 by CMS for the time period between August 1st, 2013 and December 31st, 2013. Prior to the Sunshine Act, organizations like the National Institutes of Health and the FDA required pharmaceutical manufacturers to report financial relationships with physicians, but the threshold to report

8. Larkin, Ian, Desmond Ang, Jonathan Steinhart, Matthew Chao, Mark Patterson, Sunita Sah, Tina Wu et al.. "Association between academic medical center pharmaceutical detailing policies and physician prescribing." Jama 317, no. 17 (2017): 1785-1795.

payments were high for both organizations ($5,000 and $50,000 respectively). [9] One of the crucial components of the Sunshine Act for researchers is the requirement to record and publish data. To establish transparency on the relationship between pharmaceutical marketing to physicians, CMS publishes these payments in the Open Payments database, which is freely accessible on the CMS website.[10]

Since the Open Payments database was released for public exploration and analysis, there have been many recent studies that have examined payment trends from PSRs to physicians by linking the Open Payments database to Medicare Part D data. Medicare Part D is the prescription drug coverage component of Medicare, which is available to all Medicare beneficiaries and like the Open Payments database, this data is available for download on the CMS website.[10]

In May 2016, Yeh et al. examined the relationship between PSR marketing and prescribing in the context of statin prescribing in Massachusetts. The researchers linked the 2013 Open Payments database to Medicare Part D claims data and used linear regression to "analyze the association between the intensity of physicians' industry relationships (as measured by total payments) and their prescribing practices, as well as the effects of specific types of payments." The analysis found prescribers that received statin-related payments were more likely to prescribe brand-name statins rather than cheaper, non-promoted generic alternatives.[11]

In June 2016, Perlis et al. linked 2013 Open Payments data with the Medicare Part D Prescriber File, which is a CMS database that contains physician claims, beneficiaries, and other data for particular drugs in the scope of Medicare Part-D. The scope of their study was more broad and found that among the "12 months of prescribing data from more than 700,000 U.S.

9. Parisi, Thomas J., Isabella M. Ferre, and Harry E. Rubash. "The basics of the sunshine act: how it pertains to the practicing orthopedic surgeon." JAAOS-Journal of the American Academy of Orthopedic Surgeons 23, no. 8 (2015): 455-467.
10. Open Payments. Baltimore, MD: Centers for Medicare & Medicaid Services; 2015. https://openpaymentsdata-origin.cms.gov/
11. Yeh, James S., Jessica M. Franklin, Jerry Avorn, Joan Landon, and Aaron S. Kesselheim. "Association of industry payments to physicians with the prescribing of brand-name statins in Massachusetts." JAMA internal medicine 176, no. 6 (2016): 763-768.

physicians, including analysis of nearly 400,000 individuals within 12 specialties, we find that receipt of industry payments is associated with greater prescription cost per beneficiary.” [12]

In August 2016, DeJong et al. performed a cross-sectional analysis of meal payments from the 2013 Open Payments database and the 2013 Medicare Part D Prescriber File that focused on four target drugs (osuvastatin, nebivolol, olmesartan, and desvenlafaxine). The researchers used a “multivariable grouped logistic regression models with binomial physician-level prescribing data” that measured the “the association between the number of days that a physician received meals related to target drugs and his or her prescribing rate of the promoted drug as a proportion of prescriptions in the class.” As per the other studies, the researchers reported based on their analysis that “physicians who received meals related to target drugs had a greater mean prescribing volume than those who did not.” [13]

2.4. The Relationship Between Open Payments and Opioid Prescribing

While existing studies like DeJong et al. have established a relationship between payments to physicians in the Open Payments database and physician prescribing, there is little research focusing on Open Payments for opioid products and their link to opioid prescribing in the Medicare Part D program.

In 2017, Hadland et al. (2017) integrated and analyzed Open Payments data from 2013-2015 in an effort to uncover trends among physicians that were marketed opioid products specifically. Their analysis used summary statistic techniques like medians, means, and interquartile ranges of physician subgroups that received opioid-related payments, such as payment types, the US state associated with the physician’s practice, and the physician’s primary specialty (primary care, anesthesiology, etc.). Based on their research, 1% of physicians received 82.5% of total payments in dollars. The highest payments in terms of amount of US dollars were

12. Perlis, Roy H., and Clifford S. Perlis. "Physician payments from industry are associated with greater Medicare Part D prescribing costs." PloS one 11, no. 5 (2016): e0155474.
13. DeJong, Colette, Thomas Aguilar, Chien-Wen Tseng, Grace A. Lin, W. John Boscardin, and R. Adams Dudley. "Pharmaceutical industry–sponsored meals and physician prescribing patterns for Medicare beneficiaries." JAMA internal medicine 176, no. 8 (2016): 1114-1122.

for speaking engagements and the highest frequency of payments was for food and beverage payments. Most notably, one in eleven US physicians received opioid payments, including one in five primary care physicians. Hadland et al. (2017) was one of the earliest studies to specifically examine opioid payments to physicians using the Open Payments database.[14]

In 2018, Hadland et al. (2018) published a research letter in JAMA Internal Medicine entitled "Association of Pharmaceutical Industry Marketing of Opioid Products to Physicians with Subsequent Opioid Prescribing," which extended their prior study from 2017 to examine the relationship between opioid payments and opioid prescribing. The researchers found that physicians receiving opioid payments were associated with 9.3% greater opioid claims than those that did not receive payments for opioids, based on a multiple linear regression model that adjusted for 2014 opioid prescription claims and change in total claims between 2015 and 2014. The researchers importantly emphasize that this type of observational study cannot establish causality. In fact, an alternative explanation could be that prescribers with a greater number of claims are targeted specifically by opioid manufacturers to maintain existing prescribing behaviors.[15]

While existing literature on the relationship between opioid Open Payments and Medicare Part D Opioid prescribing examines physician subgroups like payment types, the US state associated with the physician's practice, and the physician's primary specialty, there is a gap in the literature in regard to examining the predictive effect of other physician characteristics that may make them more likely to prescribe more opioid products. For example, it could be the case that a physician's gender, geographic area associated with their practice (urban vs. rural), and prescribing volume could be statistically significant predictors of opioid prescribing in addition to

14. Hadland, Scott E., Maxwell S. Krieger, and Brandon DL Marshall. "Industry payments to physicians for opioid products, 2013–2015." American journal of public health 107, no. 9 (2017): 1493-1495.
15. Hadland, Scott E., Magdalena Cerdá, Yu Li, Maxwell S. Krieger, and Brandon DL Marshall. "Association of pharmaceutical industry marketing of opioid products to physicians with subsequent opioid prescribing." JAMA internal medicine 178, no. 6 (2018): 861-863.

receiving opioid Open Payments. Using these physician characteristics to build a profile of prescribers could be valuable in understanding predictors of opioid prescribing.

3. Data and Methods

3.1. Open Payments

Open Payments is a comprehensive database maintained and hosted online by CMS established by the Sunshine Act that provides transparency between nature of the financial relationship between the healthcare industry and physicians. The versions of the database are compiled based on the year of the payment transaction. Open Payments was first published in 2014 for a partial year of 2013 transactions and the latest version of Open Payments is for transactions from the year 2017. The focus of this analysis is the relationship between opioid prescribing based on prior year opioid claims; due to 2016 opioid claims being the latest year of claims data, only 2015 Open Payments were used. According to CMS interactive fact sheet on the 2015 Open Payments database, over $8.42 billion of payments were exchanged, with $2.7 billion of these payments being non-research payments[16].

The database contains fields that pertain to data about the physician or hospital receiving the payment, data about the manufacturer or group payer making the payment, and data about the payment or payments themselves, including the count and amount of payments, the drugs that were marketed during the transaction (between 1-5 drugs listed per database record), and the nature of payment. Table 1 examines the frequency of Opioid Payments vs. Total Payments for all available natures of payment in the Open Payments data. The most prevalent form of payment for both total payments and only opioid payments is Food and Beverage Payments (meal payments). The following example provided by CMS categorizes a typical meal payment: "A

[16] "The Facts About Open Payments Data - Open Payments Data - CMS | CMS Open Payments Data." OpenPaymentsData.CMS.gov. Accessed December 16, 2018. https://openpaymentsdata.cms.gov/summary.

sales person from a drug manufacturer asks a physician if they can talk with them about a new drug. They meet over lunch, and the salesperson pays for the meal.” [17][18]

Given the prevalence of this type of this type of transfer of funds from PSRs to physicians in the context of opioid payments, meal payments are one of the primary variables used in the analysis. ‘Non-meal payments’, which are a variable generated based on a compilation of all other natures of payment into one categorization, are used in the analysis as a control variable. In addition to subsetting the data based on meal and non-meal payments, the data were subset to only include opioid payments and meal payments in the United States. Opioid payments were identified by using names of brand and generic opioids in CMS’s 2013-2015 Opioid Drug List. A database record was included if an opioid product was any of the five possible marketed products listed for any one database record. Since Open Payments data are at the transaction-level, the data were grouped by physician.

3.2. Medicare Part D Opioid Claims

The Medicare Part D Prescriber Summary file is a public CMS database that displays the opioid prescribing rates of health care providers that prescribe opioids through the Medicare Part D program. The database contains demographic information about health care providers and information about claims, including total claims, opioid claims, and extended release opioid claims. Medicare Part D is the prescription drug coverage component of Medicare, which comprises about 70% of patients covered by Medicare. As mentioned by CMS, this data does not include patients that are covered by Medicaid or commercial insurance providers. For privacy reasons, data are redacted in situations where there are fewer than 10 opioid claims for any one health care provider[19].

[17] "Natures of Payment." CMS.gov Centers for Medicare & Medicaid Services. September 24, 2014. Accessed December 16, 2018. https://www.cms.gov/OpenPayments/About/Natures-of-Payment.html.
[18] "General Payment Data – Detailed Dataset 2015 Reporting Year | CMS Open Payments Data." OpenPaymentsData.CMS.gov. Accessed December 16, 2018. https://openpaymentsdata.cms.gov/dataset/General-Payment-Data-Detailed-Dataset-2015-Reporti/7zxq-8x42.
[19] "General Payment Data – Detailed Dataset 2015 Reporting Year | CMS Open Payments Data." OpenPaymentsData.CMS.gov. Accessed December 16, 2018. https://openpaymentsdata.cms.gov/dataset/General-Payment-Data-Detailed-Dataset-2015-Reporti/7zxq-8x42.

Table 1 – Open Payment Natures of Payment, Total Payments vs. Opioid Payments

Nature of Payment	Total Payments	Opioid Payments
Food and Beverage	10,088,333 87.4%	199,906 93.2%
Travel and Lodging	585,395 5.1%	3,310 1.5%
Education	293,828 2.5%	2,684 1.3%
Compensation for services other than consulting, including serving as faculty or as a speaker at a venue other than a continuing education program	275,721 2.4%	7,848 3.7%
Consulting Fee	143,970 1.2%	570 0.3%
Gift	70,543 0.6%	76 0.0%
Honoraria	20,930 0.2%	111 0.1%
Compensation for serving as faculty or as a speaker for a non-accredited and noncertified continuing education program	15,602 0.1%	6 0.0%
Royalty or License	15,051 0.1%	14 0.0%
Grant	10,134 0.1%	6 0.0%
Space rental or facility fees(teaching hospital only)	9,444 0.1%	14 0.0%
Entertainment	6,944 0.1%	- 0.0%
Current or prospective ownership or investment interest	4,127 0.0%	- 0.0%
Compensation for serving as faculty or as a speaker for an accredited or certified continuing education program	1,791 0.0%	- 0.0%
Charitable Contribution	1,723 0.0%	- 0.0%

3.3. Data Aggregation and Analysis Variables

The Open Payments and Medicare Part D claims databases do not share a primary key or other unique identifier. Therefore, to join these two databases together, a combination of physician name and zip code were used to match records. The scope of the analysis only included physicians that received at least one opioid payment and therefore any unmatched records were not included. The data were matched and integrated using R Studio software and the ‘sqldf’ package, which enables the user to run Transact-SQL statement scripts within an R development environment. [20][21][22] Table 2 contains a data dictionary of the variables utilized for analysis.

Table 2 – Analysis Data Dictionary

Variable Name	Variable Type	Description
NPI	Primary Key	National Provider ID.
2016 Opioid Claims	Continuous	2016 Opioid Claims. Log base 10 transformed for analysis.
2015 Opioid Claims	Continuous	2015 Opioid Claims. Log base 10 transformed for analysis.
2015 Meal Payments	Continuous	2015 Meal Payments. Log base 10 transformed for analysis.
2015 Non-Meal Payments	Continuous	2015 Non-Meal Payments. Log base 10 transformed for analysis.
Gender	Categorical	Physician Gender.
Region	Categorical	Physician US state region.
Specialty Group (n=11 variables)	Binary	Dummy variables for each specialty group. Variables include Family Practice, Internal Medicine, Emergency & Surgery Specialties, Pain Specialties, Physical Medicine and Rehabilitation, Neurology, Anesthesiology, Oncology Specialties, Rheumatology, General Practice, Other Specialties (n=58)

3.4. Data Transformation for Analysis

Before completing any analyses, opioid claims and opioid payments data were logarithmically transformed at base 10 (x+1) due to both variables' right skewed distributions and their use in parametric statistical methods, such as ANOVA and multivariate linear regression. These transformations were both consistent with the methodology outlined by Hadland et al. and yielded residual and quantile-quantile plots that were closest to normal relative to other data transformations. Parametric statistical methods were used in favor of non-parametric methods due to their robustness and familiarity of interpretability with academics across various disciplines.

[20] R Core Team (2017). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.
[21] RStudio Team (2015). RStudio: Integrated Development for R. RStudio, Inc., Boston, MA URL http://www.rstudio.com/.
[22] G. Grothendieck (2017). sqldf: Manipulate R Data Frames Using SQL. R package version 0.4-11. https://CRAN.R-project.org/package=sqldf

4. Results

Table 3 – Multivariate Linear Regression Models Predicting Opioid Claims

Model Predictors	Model 1	Model 2	Model 3	Model 4
2015 Meal Pay Count	0.0414*** (0.0049)	0.0350*** (0.0037)	0.0432*** (0.0049)	0.0227*** (0.0053)
2015 Non-Meal Pay Count	-0.0216* (0.0099)	-0.0182* (0.0076)	-0.0208* (0.0099)	-0.0256** (0.0099)
2015 Opioid Claims	0.9633*** (0.0028)	0.9682*** (0.0022)	0.9604*** (0.0028)	0.9532*** (0.0030)
Male	-	-0.0024 (0.0029)	-	-
Northeast	-	-	-0.0136** (0.0049)	-
South	-	-	0.0098* (0.0041)	-
West	-	-	-0.0097* (0.0049)	-
Family Practice	-	-	-	0.0600*** (0.0078)
Emergency/Surgery	-	-	-	0.0405*** (0.0087)
Internal Medicine	-	-	-	0.0536*** (0.0080)
Oncology	-	-	-	0.0603*** (0.0104)
Pain	-	-	-	0.1093*** (0.0099)
Rehabilitation	-	-	-	0.0935*** (0.0097)
Neurology	-	-	-	0.0334*** (0.0100)
Anesthesiology	-	-	-	0.0838*** (0.0107)
Rheumatology	-	-	-	0.0725*** (0.0118)
General Practice	-	-	-	0.0382** (0.0147)
Intercept	0.0355*** (0.0064)	0.0509*** (0.0053)	0.0418*** (0.0072)	0.0124 (0.0088)
Degrees of Freedom	29,517	26,458	29,514	29,507
Adjusted R2	0.8334	0.9021	0.8336	0.8343
F-test	49,230	60,930	24,650	11,440

Significance codes: 0 ‘***’, 0.001 ‘**’, 0.01 ‘*’ 0.05
Standard Errors in parentheses

4.1. Opioid Payments vs. Opioid Claims

The purpose of this analysis is to determine whether there is an association between opioid meal payments from PSRs to physicians and subsequent physician opioid prescribing. After establishing the nature of this relationship, subsequent analyses examine if understanding of this association can enhanced through considering physician demographic characteristics like physician gender, state of practice, and specialty. Table 3 contains the linear regression coefficients, standard error, and significance levels for Models 1, 2, 3, and 4.

Model 1 is based on a model mentioned by Hadland et al. when examining the relationship between opioid prescribing and opioid meal payments. The multivariate linear regression model uses 2015 meal payments, 2015 non-meal payments, and 2015 opioid payments as predictors of opioid claims. 2015 opioid claims were added as an additional covariate control variable to help prevent omitted variable bias for physicians who prescribed many opioids in 2016 due to also having prescribed many in opioids 2015 rather than this being explained by meal payments. 2015 Non-Meal Payments include all other payments to physicians that don't include meal payments (e.g. consulting, lodging) and this variable was included as a control variable to control for any other types of payments made to physicians to influence their prescribing behavior.

This model confirms the findings of Hadland et al. in that opioid meal payments are predictive of opioid payments ($p < 0.01$). More specifically, after the variables are un-transformed, an increase of 10 opioid meal payments are associated with an increase of 12.5898 opioid claims after controlling for non-meal payments and prior year opioid prescribing. The adjusted R^2 of 0.8334 is quite high and indicates the model covariates can jointly explain 83.34% of the variance in the outcome of opioid claims. Not only does this result provide confirmatory evidence that opioid meal payments are associated with opioid claims, but it also reproduces existing research with data from a year after the original study, which provides further evidence to support the findings of Hadland et al.

4.2. Enhancing understanding of the Opioid Payments vs. Opioid Claims Relationship

Subsequent analyses introduce physician gender, region of practice, and specialty to help further understand the association between opioid payments and claims. Each of the analyses first explore the relationship between only the respective subgroups and opioid claims using analysis of variance (ANOVA), Tukey Honestly Significant Difference tests (Tukey HSD test), and boxplots visualizations. Then, multivariate linear regression models use the subgroups as additional covariate predictors to enhance the existing relationship explored in Model 1.

4.3. Physician Gender & Opioid Payments vs. Opioid Claims

Figure 1 – Opioid Claims Quantile Distributions, Gender[23][24]

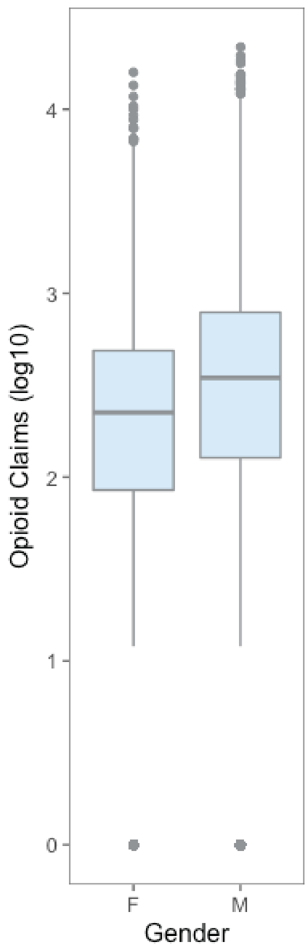

Table 4 – Physician Summary Statistics, Gender

		Opioid Claims	
Gender	n	Median	Mean
Male	21,332	346	694
Female	5,630	223	442

One-way ANOVA p-value = almost 0

[23] H. Wickham. ggplot2: Elegant Graphics for Data Analysis. Springer-Verlag New York, 2009.
[24] Jeffrey B. Arnold (2017). ggthemes: Extra Themes, Scales and Geoms for 'ggplot2'. R package version 3.4.0. https://CRAN.R-project.org/package=ggthemes

When comparing the difference in means of opioid claims between female physicians and male physicians using an ANOVA, there is a statistically significant difference at all conventional levels between the group means ($p < 0.01$). This relationship is also true when comparing male and female opioid claims from a quartile perspective. As can be seen visually in Figure 1 and in Table 4, it can be observed that male physicians have higher median opioid claims than female physicians.

Model 2 explores whether this difference influences the ability of opioid meal payments to predict opioid claims between genders. This model contains the same covariates as Model 1 with an additional variable added that identifies whether the physician is male or female. Interestingly, the coefficient of the gender variable is not statistically significant at any conventional level ($p > 0.1$). This result is a valuable insight, as it shows that there is no significant difference in prescribing behavior between male and female physicians and the difference in this relationship that can be observed in Figure 1 and Table 4 can actually be attributed to not controlling for non-meal payments and prior year opioid claims in these simpler models. Practically speaking, this result provides evidence to suggest that males are no less susceptible than females when it comes to being influenced by pharmaceutical marketing. If gender is viewed in the model as a control variable, the addition of this variable makes the model explain 90.21% of the variance in the outcome of opioid claims. However, it is important to note that the degrees of freedom are less in this model given a number of physicians not having gender disclosed which likely biases this type of comparison between Model 1 and Model 2.

4.4. Physician Region of Practice & Opioid Payments vs. Opioid Claims

Figure 2 – Opioid Claims Quantile Distributions, Region

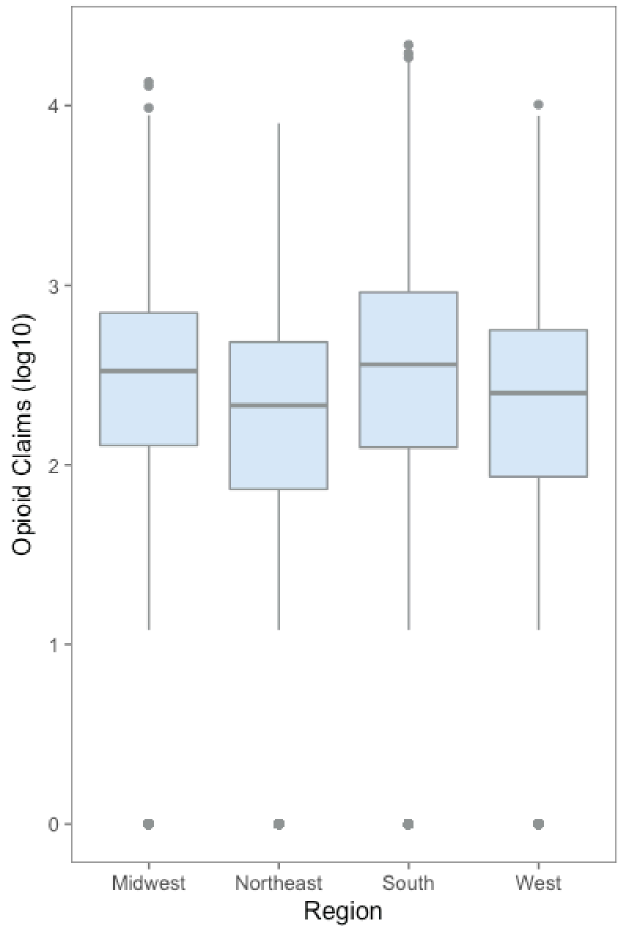

Table 5 – Physician Summary Statistics, Region

		Opioid Claims	
Region	n	Median	Mean
Northeast	5,539	213	391
South	12,546	361	828
West	5,640	332	579
Midwest	6,470	250	449

One-way ANOVA p-value = almost 0

Tukey HSD p-values almost zero for all group comparisons

To determine whether geographic region is an important factor when considering opioid prescribing, the state of a physician's practice as identified by CMS was classified as Northeast, Midwest, South, and West. When comparing the difference in means of opioid claims between physicians from Northeast states, Midwest states, South states, and West states using an ANOVA, there is a statistically significant difference between the population means ($p < 0.01$). If this relationship is further examined using a Tukey HSD test, there is a statistically significant difference between all possible combinations of the group means. This relationship is also true when comparing regional opioid claims from a quartile perspective. As can be seen visually in Figure 2, it can be observed that physicians from states in the South have the highest median opioid claims, while physicians from the Northeast have the lowest median opioid claims and no statistical outliers greater than 1.5 standard deviations from the median.

Model 3 explores whether this difference influences the ability of opioid meal payments to predict opioid claims between these regional groups. Model 3 contains the same covariates as Model 1 with a categorical variable for each geographic region, except the Midwest region, which was excluded by statistical software to avoid the dummy variable trap. The Northeast, South, and West coefficients are all statistically significant at the 5% significance level. However, the effect sizes of the regional coefficients are closer to zero, which suggest there is actually not much of a meaningful difference between geography and opioid claims. For Northern states, which has the largest absolute effect size, going from being a non-Northern state to being a Northern state is associated with a -0.0136 decrease in logged opioid claims (about a 1 opioid claim decrease per 10 opioid meals if untransformed). While this appears to contrast conventional wisdom that southern states are associated with higher opioid abuse, this could be confounded by the propensity of opioid manufacturers to target specific geographic regions with physician marketing versus others, which may differ from geographic regions that have a higher propensity of opioid abuse and fatalities.

4.5. Physician Specialty & Opioid Payments vs. Opioid Claims

Figure 3 – Opioid Claims Quantile Distributions, Specialty

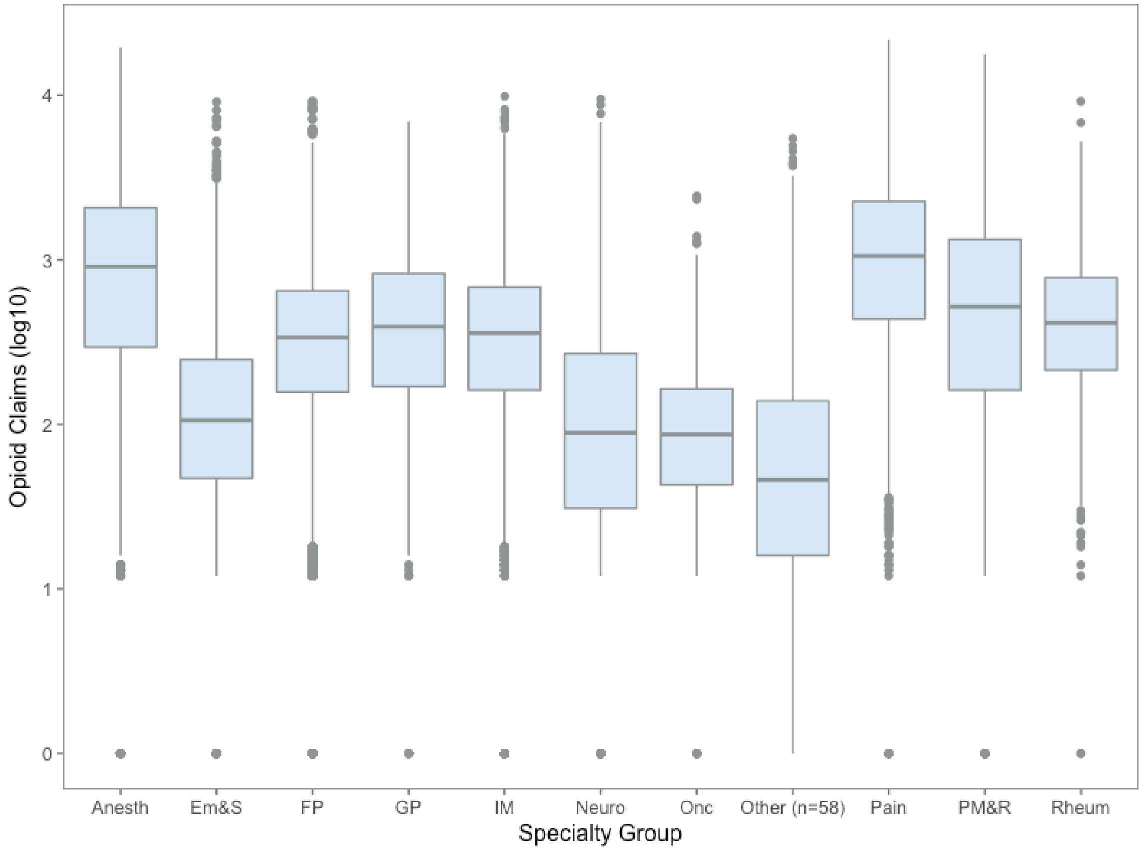

Table 6 – Physician Summary Statistics, Specialty

		Opioid Claims	
Specialty Group	n	Median	Mean
Family Practice	9,735	336	507
Internal Medicine	6,853	358	538
Emergency & Surgergy Specialties	2,799	104	252
Pain Specialties	2,051	1,052	1,752
Physical Medicine and Rehabilitation	1,905	517	1,071
Neurology	1,486	88	356
Anesthesiology	1,321	907	1,591
Oncology Specialties	1,218	86	134
Rheumatology	815	413	641
General Practice	432	392	665
Other Specialties (n=58)	1,593	45	199

One-way ANOVA p-value = almost 0

Tukey HSD p-values almost zero for 49/55 group comparisons

A physician's specialty is a crucial factor to consider when analyzing physician prescribing activity. The nature of physician prescriptions in terms of type, total quantity, and quantity relative to other products are different from a functional perspective for emergency room doctors versus dentists versus other types of doctors. When comparing the difference in means and quantile distributions, this conventional wisdom is shown to be true. An ANOVA between each specialty subgroup shows a statistically significant difference at all conventional levels between the group means ($p < 0.01$). Further, a Tukey HSD test reveals a statistically significant difference between all but 6 out of 55 possible combinations of the group means. As can be seen visually in Figure 3, pain specialists have the highest median opioid claims only rivaled by Anesthesiologists. Perhaps surprisingly, the median opioid claims for Emergency and Surgery specialties is one of the lowest; however, there are certainly still many high prescribers that are represented as statistical outliers for that particular distribution.

Model 4 explores whether particular physician specialties influence the ability of opioid meal payments to predict opioid claims. This model contains the same covariates as Model 1 with dummy variables for each physician specialty group. Unlike the gender and regional models, specialty covariates are all significant at all conventional levels ($p <0.01$). As expected from conventional wisdom, pain specialties have the largest model coefficient. In this way, going from being a non-pain specialist to a pain specialist is associated with an increase in 1.28 opioid claims after controlling for factors like opioid payments, prior year opioid claims, and other top physician specialties. This could indicate that pain physicians are more receptive to pharmaceutical marketing for opioids than other specialties, which could be a function of their medical specialization and the use of opioids as a common treatment for pain.

5. Conclusion

The purpose of this analysis is to determine whether there is an association between opioid meal payments from PSRs to physicians and subsequent physician opioid prescribing. After establishing the nature of this relationship, subsequent analyses examined if understanding of this association could be enhanced through considering physician demographic characteristics like physician gender, state of practice, and specialty.

The findings of the analysis confirm that there is an association between opioid claims and opioid meal payments after controlling for non-meal payments and prior year opioid claims. The analysis found that specialty was an important predictor of opioid claims and that pain management specialists and physicians in rehabilitation-based specialties are associated with higher opioid claims. The analysis did not find much evidence to suggest this relationship is different based on the physician gender or region of practice.

5.1. Limitations of Research

One of the limitations of the research is the CMS Medicare Part D claims data in terms of the data's scope and ability to operationalize its measurement of opioid prescribing. This data from a methodological perspective does not provide a complete record of opioid claims due to the redaction of data in situations where there are fewer than 10 opioid claims for any one health care provider. While this data is the most widely used source of data in prior research examining the association between pharmaceutical marketing and physician prescribing in recent years, it is not a perfect measure of prescribing. These claims as a measure exclude prescribing that is processed through Medicaid and commercial insurance providers. PSR marketing is intended to influence all physician prescribing as opposed to only Medicare prescribing and therefore, the data is missing part of the analyses' intended outcome variable due to the lack of availability of this data.

Another limitation of the research is the error associated with identifying opioid payments in the Open Payments data and joining the opioid payments to the opioid claims data. While NDC numbers were a field provided by CMS in the Open Payments database, these identifiers were often missing and were otherwise in various formats that could not be standardized for systematic matching. Therefore, opioid payments were identified by using names of brand and generic opioids in CMS's 2013-2015 Opioid Drug List. Due to this less precise method, a percentage of human error is likely introduced. Additionally, the Open Payments and Medicare Part D claims databases do not share a primary key or other unique identifier. Therefore, to join these two databases together, a combination of physician name and zip code were used to match records, which likely introduces a percentage of human error of both unmatched records and false positive matches.

Finally, it is crucial to emphasize analysis design limitations. Medicare Part D data is aggregated by year and therefore, examining Open Payments in year *n* and comparing to opioid claims in year *n+1* are the only way to examine opioid payment outcomes. It could the case that opioid payments have a much greater effect on physicians a week or month after payment, but the effect diminishes after longer time periods. The current scope of the CMS data is not able to answer this type of inquiry. Also, any associations described during the course of the analysis do not prove causality or directionality. While it was observed that opioid payments are associated with opioid claims, this could mean that payments influenced claims or that doctors that prescribe opioids were targeted by opioid manufacturers and therefore were more predisposed to these claims by design. This research also describes an observational analysis rather than an RCT and therefore, there is bias in the model that cannot be controlled.

5.2. Future Avenues of Research

Given there are so few analyses that examine the relationship between opioid meal payments and opioid claims, there are many avenues of future research. One avenue could be to replicate the analysis by replacing the opioid claims data with commercial insurance prescriptions. The challenge associated with this type of analysis is that the data are not publically available and must be purchased from retail data aggregators like IMS Health or Symphony Health. A similar avenue of research could be to replicate the analysis by replacing the opioid claims data with opioid fatalities or another variable that identifies opioid abuse to gain an understanding of opioid prescriptions that are used as prescribed versus being abused by patients. A challenge associated with this analysis may be accounting for opioids not manufactured by pharmaceutical companies that contribute to the opioid epidemic, such as heroin and illicitly manufactured synthetic opioids.

Probably the most impactful future avenue of research would be to design an RCT that can reduce as much bias as possible in regard to identifying the effect of pharmaceutical marketing of opioids to doctors and those doctors subsequent prescribing of medications. RCTs have been used in the context of measuring prescribing behavior in relation to other drugs, but not opioids to the author's knowledge. A design of such a study could be varied, but would require randomization of doctors or medical students into a control group and one or more treatment groups. Treatment groups could have some kind of restriction of opioid prescribing, have stricter rules against pharmaceutical marketing, or be encouraged to prescribe non-opioid anti-inflammatory drugs, while the control group may not have such restrictions.

5.3. Policy Implications

This analysis provides evidence to suggest that PSR efforts to market to physicians are creating the desired effect of increasing opioid prescribing. From a policy perspective, the analysis provides policymakers with further evidence to support the Sunshine Act, Physician Data Restriction Program, and other programs to make it more difficult for manufacturers to influence physicians. This argument is made to varying degrees in numerous other studies that examine pharmaceutical marketing, including Hadland et al., who reported "federal and state governments should consider legal limits on the number and amount of payments." A precise solution is unclear, but given the opioid epidemic is considered a Public Health Emergency by HHS, this research can help justify funding for additional avenues of research through grants. This would be a step in the right direction for ultimately furthering the fight against opioid epidemic through data-driven research and understanding.

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7. Curriculum Vita

Christopher Pfeiffer is a Senior Business Analyst at Tegra Analytics, a data analytics consultancy that advises clients within the pharmaceutical, medical device, and life science industries. During his six-year tenure at Tegra, Christopher has lead and managed a variety of projects, including sales forecasting and sizing models, account targeting and segmentation, incentive compensation design, and sales effectiveness analyses. He also provides QA/QC support for clinical trials, including studies that led to the FDA approval of OraVerse® and Kovanaze® in pediatric dental patients and acts as a research assistant on industry trends, including co-authoring a company whitepaper entitled *Oncology Product Portfolio Forecast using Monte Carlo Methods*.

In addition to his work at Tegra Analytics, Christopher is a candidate for a Master of Science in Government Analytics at The Johns Hopkins University, with a specialization in Statistical Analysis. Prior to his graduate studies, Christopher graduated from La Salle University in Philadelphia, PA, where he earned a Bachelor of Science in Business Administration with a specialization in Finance and a minor in Economics. During his time as an undergraduate, he was a member of La Salle's Business Scholar's Co-op Program, which enabled him to complete co-ops at Johnson & Johnson and SAP.

Christopher was raised in Warwick, PA and resides in Memphis, TN. He is a member of the Western Tennessee Chapter of the American Statistical Association and in his spare time enjoys ukulele, board games, travel, and spending time with friends and family.